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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,361	09/22/2003	Denis M. Boyle	6794A-000009/US/CPA	4467

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HARNESS, DICKEY & PIERCE, P.L.C.
P.O. BOX 8910
RESTON, VA 20195

EXAMINER	
DESAI, ANAND U	
ART UNIT	**PAPER NUMBER**
1656	
MAIL DATE	**DELIVERY MODE**
10/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,361	BOYLE ET AL.	
	Examiner	Art Unit	
	Anand U. Desai, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,8,12,15-17,20,23,26,31,34,37,40,43,51,54 and 205-217* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,12,15-17,20,23,26,31,34,40,54,205,208,216 and 217* is/are rejected.

7)☒ Claim(s) *43,51,206,207 and 209-215* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *20070730*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 30, 2007 has been entered.

2. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 43, 51, 54, and 205-217 are currently pending and are under examination.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on July 30, 2007 is being considered by the examiner. The WO 96/40731 reference is being placed in the Foreign Patent Documents section of the IDS form.

Oath/Declaration

4. A new oath or declaration is required because it is not apparent that the pending application is a Continuation-In-Part of non-provisional U.S. Application Interim Serial No. P-107,891. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly

identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

Response to Remarks

The examiner acknowledges that the applicants have stated that a new Oath and Declaration will be provided under separate cover.

Claim Rejections - 35 USC § 112, 1st paragraph, enablement rejection

5. Claims 1-5, 8, 12, 15-17, 20, 23, 26, 31, 34, 37, 40, 54, 205, 208, 216, and 217 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a process for decreasing a level of aggregate of pegylated protein isoforms by anion exchange chromatography using an anion exchange resin under sufficient conditions to decrease said level of said aggregate, wherein the protein is selected from the group consisting of human growth hormone antagonist comprising B-2036 amino acid sequence, pegylated isoforms of B-2036 identified as PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, PEG-9, trisulfide impurity of B-2036 and des-phe impurity of B-2036, does not reasonably provide enablement for a process using anion exchange chromatography with any protein growth hormone antagonist. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are rejected because of undue experimentation to practice the claimed method for the genus of growth hormone antagonist peptides. The undue experimentation arises due to the unpredictability based on the differing conditions of starting materials, such as the genus of

growth hormone antagonist peptides being claimed, and due to the different structures of the peptides encompassed by the claims. The claims are drawn to any protein growth hormone antagonists.

In *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) eight factors should be addressed in determining enablement.

While the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. The language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims. This can be done by making specific findings of fact, supported by the evidence, and then drawing conclusions based on these findings of fact. For example, doubt may arise about enablement because information is missing about one or more essential parts or relationships between parts which one skilled in the art could not develop without undue experimentation. In such a case, the examiner should specifically identify what information is missing and why one skilled in the art could not supply the information without undue experimentation. See MPEP § 2164.06(a). References should be supplied if possible to support a prima facie case of lack of enablement, but are not always required. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). However, specific technical reasons are always required.

1) The nature of the invention: the instant claims are directed to a process for decreasing a level of aggregate of pegylated protein isoforms by anion exchange chromatography using an anion exchange resin under sufficient conditions to decrease said level of said aggregate, wherein the pegylated protein is a collection of isoforms of pegylated protein of any growth hormone antagonist. Claims 43, 51, 206, 207, 209, 210, and 211-215 recite the growth hormone antagonist as the B-2036 amino acid sequence, and pegylated isoforms of B-2036 identified as PEG-1, PEG-2, PEG-3, PEG-4, PEG-5, PEG-6, PEG-7, PEG-8, PEG-9, trisulfide impurity of B-2036 and des-phe impurity of B-2036, which are separated using an anion exchange column chromatography step.

3) The predictability or unpredictability of the art: & 6) The quantity of experimentation necessary: & 7.) The state of the prior art: the prior art has shown a large quantity of experimentation is often necessary to overcome the unpredictable nature of protein purification. Burling (U.S. Patent 5,149,647) describes the process of extracting pure fractions of lactoperoxidase and lactoferrin from milk serum, using first microfiltration, and then cation-exchange chromatrography (see claims 1-4). Koide et al. (U.S. Patent 5,290,685) cites Naito and Suzuki that disclose the fractionation of phosphopeptides using ion exchange at an acidic pH of 2.5 (see col. 1, lines 36-42). Koide et al. also cites the use of ultrafiltration in a method of separating phosphopeptides (see col. 1, lines 57-65). Mozaffar et al. (U.S. Patent 6,096,870) describe the elution and sequential separation of four proteins from non-α-lactoglobulin fraction of liquid whey using a strong S-cationic exchange resin, where the eluted proteins are further passed through a 5,000-10,000 molecular weight cut-off membrane to concentrate the protein and remove salt residues (see col. 24, lines 25-47).

Therefore, the unpredictability arises due to the differing conditions of starting materials, such as the genus of growth hormone antagonist being claimed, and due to the different structures of the growth hormone antagonist that require different purification steps.

Consequently, there would be a large quantity of experimentation necessary to determine what conditions are required to decrease a level of aggregate of pegylated protein isoforms.

4) The amount of direction or guidance presented: & 5) The presence or absence of working examples: the specification is devoid of any examples that process any peptides other than B-2036 antagonists using any particular anion exchange resins.

How would one of skilled in the art use the method if it is unknown what peptide antagonist is being used? How would one of skill in the art know which anion exchange resin to use or what pH to have to decrease aggregates?

8.) Level of skill in the art: the level of skill in this art is high, at least that of a doctoral scientist with several years of experience in the art.

In consideration of the Wands factors, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Objections

6. Claims 43, 51, 206, 207, and 209-215 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

7. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U. Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Kathleen Kerr Bragdon can be reached on (517) 272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

October 11, 2007

AD
/Anand Desai/
Art Unit 1656
Patent Examiner